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ADVANCES IN THE TREATMENT OF MULTIPLE MYELOMA: SURVIVAL ANALYSIS OF 560 PATIENTS IN A TWENTY-FIVE YEARS PERIOD IN A SINGLE CENTER

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Background. Therapy of multiple myeloma (MM) has been greatly advanced by introduction of autologous hematopoietic stem cell transplantation (AHSCT) in 90's, and appearance of new potent drugs thalidomide, bortezomib and lenalidomide in the last decade. **Aims.** to assess the efficacy of new treatment modalities on survival of MM patients treated at the University Hospital Center, Zagreb. PATIENTS AND **Methods.** From 1985 till 2010, 560 consecutive MM patients (pts) were analyzed. Median age at diagnosis was 60 (range 28-89) years. Pts were divided into three groups according to time period of available treatment modalities: Group one treated from 1985-1995, period prior AHSCT (n=158, median age 63 [range: 31-87]); group two treated from 1996-2001, period with AHSCT (n=139, median age 58 [range: 29-87]); and group three treated from 2002-2010, period with AHSCT+bortezomib+thalidomide (n=263, median age 60 [range: 28-89]). Each group was subdivided in two subgroups according to age at diagnosis indicating eligibility for AHSCT (<65 and ≥65 years of age). Estimated median overall survival (OS) was calculated by Kaplan-Meier method. Differences between groups were tested by 2-tailed log-rank test with p value of <. 05 being statistically significant. **Results.** Median follow-up for entire cohort was 42. 5 (range: 1-267 months). Seventy-three pts were lost from follow-up after median time of 16 (range: 1-123) months. Estimated median OS was 69 (95%CI 59. 07-78. 93) months. For groups 1 and 2, estimated median OS were 38 (95%CI 29. 44-46. 56) and 47 (95%CI 36. 06-57. 94) months respectively, while for the group 3 estimated median OS was not reached for the median follow-up of 48 (range: 1-118) months. OS was significantly different between all groups: groups 1:2 (p=0. 009), groups 2:3 (p<0. 0001), groups 1:3 (p<0. 0001) (Figure 1). When adjusted for age, significance between groups 1 and 2 was not reached (p=0. 058) although showing trends for better OS in group 2. Statistically significant difference remained between groups 1:3 and 2:3 (p<0. 0001, for each). OS for patients younger than 65 are significantly better compared to patients with 65 years or older, in all three groups. **Conclusions.** The analysis of OS clearly showed significantly better outcome for pts treated with AHSCT, especially for younger patients. In most recent time period both younger and older patients showed better OS probably due to introduction of new treatment modalities with thalidomide or bortezomib. Results of the study are in accordance with other similar retrospective analyses.

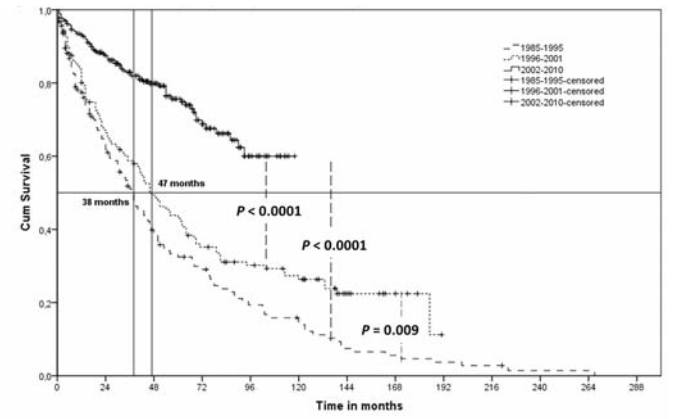

Figure 1. Overall survival for multiple myeloma patients in different periods.

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LENALIDOMIDE COMBINED WITH LIPOSOMAL DOXORUBICIN AND LOW DOSE DEXAMETHASONE (RDD) FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS: SAFETY AND EFFICACY

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Background. Multiple Myeloma treatment has considerably changed in the past decade with improvement of response rates and overall survival. Nevertheless, the best treatment regimen for relapsed patients is not standardized. Lenalidomide is approved for treatment of relapsed myeloma. Previous trials have highlighted activity of Liposomal Doxorubicin in this setting of patients. **Aims.** We asses safety and efficacy of Lenalidomide,Liposomal Doxorubicin and low dose dexamethasone (RDd) in relapsed/refractory patients. **Methods.** between June 2008 to February 2012,35 patients were enrolled. Lenalidomide(25 mg/die,day 1-21), Liposomal Doxorubicin (30mg/mq i. v. on day 1) and dexamethazone (20 mg/die, day 1, 8, 15, 22) of 28 days cycle, was administered for 6 cycles (Induction Phase,IP). Patients in CR-PR(IMWG criteria) post IP received 3 other courses of RDd as consolidation. Responder patients allowed 10 mg/die Lenalidomide (day 1-21 every 35 days) until progression or treatment intolerance. Unresponsive patients discontinued treatment. **Results.** The characteristics of enrolled patients were summarized in Table 1.

Table 1. Patient characteristics at enrollment.

Patient Characteristics	N=35
Median age, y (range)	69 (46-81)
⩾ 65 years	21(60%)
Type of Myeloma, no. (%)	
IgGL/IgGK	8 (23%)/ 12 (34%)
IgAL/ IgAK	4 (11%) / 8 (23%)
Lambda	2 (6%)
Non secer	1 (3%)
Durie Salmon stage, no. (%)	
IIIA	27 (77%)
IIA	6 (17%)
IIIB	2 (6%)
ISS, no. (%)	
I	12 (36%)
II	13 (40%)
III	8 (24%)
Median Time since initial diagnosis, months	31 (5-185)
Median number of prior therapy, no.(range)	2 (1-6)
cycles>3	9 (26%)
Prior transplant, no. (%)	17(49%)
Prior thalidomide regimens, n (%)	19 (54%)
Prior Bortezomib regimens, n (%)	24 (69%)

Nine patients (26%) were considered as high risk because of heavly pre-treatment. Nineteen (54%) and 24(69%) received,respectively,previous treatment with thalidomide or bortezomib,Seventeen patients(49%) received a previous autotransplant. The common side-effects during RDd were showed in Table 2.

Table 2. Incidence of haematological and extra-haematological toxicity.

Variable	All cases 35	WHO grade, n (%)			
		1	2	3	4
Haematological side effects					
Anemia	23 (66%)	15 (65%)	5 (22%)	3 (14%)	/
Thrombocitopenia	22 (63%)	14 (64%)	3 (14%)	5 (27%)	/
Neutropenia	33 (94%)	15 (45%)	10 (30%)	8 (26%)	/
Non-Haematological side effects					
Neuropathy	24 (69%)	19 (79%)	5 (21%)	/	/
Skin rash	4 (12%)	3 (75%)	1 (25%)	/	/
Fever	6(17%)	1	1		
Deep Venous Thrombosis	4(11%)				